
The Homeobox Transcription Factor RHOX10 Drives Mouse Spermatogonial Stem Cell Establishment.

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Public Summary:

Scientific Abstract:

The developmental origins of most adult stem cells are poorly understood. Here, we report the identification of a transcription factor-RHOX10-critical for the initial establishment of spermatogonial stem cells (SSCs). Conditional loss of the entire 33-gene X-linked homeobox gene cluster that includes RhoX10 causes progressive spermatogenic decline, a phenotype indistinguishable from that caused by loss of only RhoX10. We demonstrate that this phenotype results from dramatically reduced SSC generation. By using a battery of approaches, including single-cell-RNA sequencing (scRNA-seq) analysis, we show that RhoX10 drives SSC generation by promoting pro-spermatogonia differentiation. RhoX10 also regulates batteries of migration genes and promotes the migration of pro-spermatogonia into the SSC niche. The identification of an X-linked homeobox gene that drives the initial generation of SSCs has implications for the evolution of X-linked gene clusters and sheds light on regulatory mechanisms influencing adult stem cell generation in general.

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